SEQUENCE LISTING

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Ansari, Aslam

<120> BLOOD-BRAIN BARRIER THERAPEUTICS

<130> 9233.8DV1

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<141> 1999-10-29

<150> US 09/134,803
<151> 1998-08-14

<160> 52

<170> PatentIn version 3.2

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<220>
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<222> (6)..(6)
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<400> 1

Tyr Gly Gly Phe Met Lys
1 5

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<223> Polymer connected to epsilon-amino group

<400> 2

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1 5

<210> 3
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<220>
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<220>
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<223> Polymer connected to alpha-amino group

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1 5

<210> 4
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<220>
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<223> ACETYLATION

<220>
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<223> AMIDATION

<400> 4

Phe Arg Trp Trp Tyr Lys
1 5

<210> 5
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<220>
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<220>
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<223> AMIDATION

<400> 5

Arg Trp Ile Gly Trp Lys
1 5

<210> 6
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B1

<220>
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<220>
<221> MOD_RES
<222> (6)..(6)
<223> AMIDATION

<220>
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<222> (6)..(6)
<223> Xaa can be any naturally occurring amino acid

<400> 6

Trp Trp Pro Lys His Xaa
1 5

<210> 7
<211> 4
<212> PRT
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<220>
<223> Synthetic construct

<220>
<221> MOD_RES
<222> (4)..(4)
<223> AMIDATION

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa is either Lys or Arg

<400> 7

Trp Trp Pro Xaa
1

<210> 8
<211> 6
<212> PRT
<213> Artificial sequence

<220>
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<220>
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<223> AMIDATION

B1

<220>
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<222> (6)..(6)
<223> Xaa can be any naturally occurring amino acid

<400> 8

Tyr Pro Phe Gly Phe Xaa
1 5

<210> 9
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<220>
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<220>
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<222> (1)..(5)
<223> Amino acids are in the D-form

<220>
<221> MOD_RES

<222> (6)..(6)
<223> n is 0 or 1

<220>
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<222> (7)..(7)
<223> Xaa is Gly or the D-form of any naturally occurring amino acid

<220>
<221> MOD_RES
<222> (7)..(7)
<223> Amidation

<400> 9

Ile Met Ser Trp Trp Gly Xaa
1 5

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B1

<220>
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<222> (1)..(4)
<223> Amino acids are in the D-form

<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa is Gly or the D-form of any naturally occurring amino acid

<220>
<221> MOD_RES
<222> (6)..(6)
<223> AMIDATION

<400> 10

Ile Met Thr Trp Gly Xaa
1 5

<210> 11
<211> 4
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<213> Artificial sequence

<220>
<223> Synthetic construct

<220>
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<222> (2)..(2)
<223> Xaa is A1, wherein A1 is the D-form of Nve or Mle

<220>
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<222> (3)..(3)
<223> Xaa is B2, wherein B2 is Gly, Phe, or Trp

<220>
<221> MISC_FEATURE
<222> (4)..(4)
<223> Xaa is C3, wherein C3 is Trp or Nap

<220>
<221> MOD_RES
<222> (4)..(4)
<223> AMIDATION

<400> 11

Tyr Xaa Xaa Xaa
1

B1

<210> 12
<211> 3
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic construct

<220>
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<222> (1)..(1)
<223> Tyr has at its N-terminus a Me-x-H-y-N group, wherein x is 0, 1, or 2; and y is 0, 1, or 2, with the proviso that x and y is never greater than 2

<220>
<221> MOD_RES
<222> (1)..(2)
<223> The amine between the first Tyr and the second Tyr is methylated, wherein z is 0 or 1

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa is Xaa-z, wherein Xaa is Phe, D-Phe or NHBzl, and wherein z is 0 or 1

<220>
<221> MOD_RES

<222> (3)..(3)
<223> AMIDATION

<400> 12

Tyr Tyr Xaa
1

<210> 13
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<220>
<223> Synthetic construct

<220>
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<222> (4)..(4)
<223> Xaa is D4, wherein D4 is Lys or Arg

<220>
<221> MOD_RES
<222> (5)..(5)
<223> His is His-z, wherein z is 0 or 1

B1

<220>
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<222> (6)..(6)
<223> Xaa is Xaa-z, wherein Xaa is any naturally occuring amino acid and z is 0 or 1

<220>
<221> MOD_RES
<222> (6)..(6)
<223> AMIDATION

<400> 13

Trp Trp Pro Xaa His Xaa
1 5

<210> 14
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<220>
<223> Synthetic construct

<220>
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<222> (2)..(2)

<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 14

Tyr Xaa Phe Phe
1

<210> 15
<211> 4
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic construct

<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (4)..(4)
<223> AMIDATION

B1

<400> 15

Tyr Xaa Phe Phe
1

<210> 16
<211> 4
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<220>
<223> Synthetic construct

<220>
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<222> (1)..(1)
<223> Tyr is Tyr(N-alpha-Me), i.e. N-alpha-methyl tyrosine

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 16

Tyr Xaa Phe Phe
1

<210> 17
<211> 4
<212> PRT
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<220>
<223> Synthetic construct

<220>
<221> MOD_RES
<222> (1)..(1)
<223> Tyr is Tyr(N-alpha-Cmp), i.e. N-alpha-cyclopropylmethyltyrosine

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 17

Tyr Xaa Phe Phe
1

<210> 18
<211> 4
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<220>
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<220>
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<222> (1)..(1)
<223> Tyr is Tyr(N-alpha-hex), i.e. N-alpha-hexyltyrosine

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 18

Tyr Xaa Phe Phe
1

<210> 19
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<220>
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<222> (1)..(1)
<223> Tyr is Tyr(N-alpha-Et2), i.e. N-alpa-diethyltyrosine

<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 19

Tyr Xaa Phe Phe
1

<210> 20
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<220>
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<220>
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<222> (1)..(1)
<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 20

Tyr Xaa Phe Phe
1

<210> 21
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<220>
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<222> (1)..(1)
<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
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<223> AMIDATION

<400> 21

Tyr Xaa Phe Phe
1

<210> 22
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<220>
<223> Synthetic construct

<220>
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<222> (1)..(1)
<223> Tyr is H-Tyr(3-F), i.e. 3-fluorotyrosine

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 22

Tyr Xaa Phe Phe
1

<210> 23
<211> 4
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<220>
<223> Synthetic construct

<220>
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<222> (1)..(1)
<223> Tyr is H-Tyr(3-Cl), i.e. 3-chlorotyrosine

<220>

<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 23

Tyr Xaa Phe Phe
1

<210> 24
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<220>
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<222> (1)..(1)
<223> Tyr is H-Tyr (3-Br), i.e. 3-bromotyrosine

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

B1

<400> 24

Tyr Xaa Phe Phe
1

<210> 25
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<220>
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<222> (1)..(1)
<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>
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<222> (2)..(2)
<223> Xaa is Tic-psi-[CH2-], i.e.
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
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<222> (2)..(3)
<223> nonpetidyl bond

<400> 25

Tyr Xaa Phe Phe
1

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<220>
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<220>
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<223> Tyr is Dmt, i.e. 2,6-dimethyltyrosine

<220>
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<222> (2)..(2)
<223> Xaa is Tic-psi-[CH2-], i.e.
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (2)..(3)
<223> nonpeptidyl bond

<220>
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<222> (4)..(4)
<223> AMIDATION

<400> 26

Tyr Xaa Phe Phe
1

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<220>
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<220>
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<222> (2)..(2)

<223> Xaa is Tic-psi-[CH2-], i.e.
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (3)..(3)
<223> Phe is -NCH3]Phe, i.e. N-methylphenylalanine

<400> 27

Tyr Xaa Phe Phe
1

<210> 28
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<220>
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<222> (2)..(2)
<223> Xaa is Tic-psi-[CH2-], i.e.
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (3)..(3)
<223> Phe is -NH]Hfe, i.e. homophenylalanine

<400> 28

Tyr Xaa Phe Phe
1

<210> 29
<211> 4
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<220>
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<220>
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<222> (1)..(1)
<223> Tyr is Tyr(NMe), i.e. N-methyltyrosine

<220>
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<222> (2)..(2)

<223> Xaa is Tic-psi-[CH2-], i.e.
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
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<222> (3)..(3)
<223> Phe is -NH]Hfe, i.e. homophenylalanine

<400> 29

Tyr Xaa Phe Phe
1

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<220>
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<220>
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (3)..(3)
<223> Gly is Phg, i.e. phenylglycine

<400> 30

Tyr Xaa Gly Phe
1

<210> 31
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<220>
<223> Synthetic construct

<220>
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 31

Tyr Xaa Trp Phe
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<210> 32
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<220>
<223> Synthetic construct

<220>
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (4)..(4)
<223> AMIDATION

<400> 32

Tyr Xaa Trp Phe
1

B1

<210> 33
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<220>
<223> Synthetic construct

<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 33

Tyr Xaa His Phe
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<210> 34
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<213> Artificial sequence

<220>
<223> Synthetic construct

<220>

<221> MISC_FEATURE
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (3)..(3)
<223> Ala is 2-Nal, i.e. 3-(2'-napthyl)alanine

<400> 34

Tyr Xaa Ala Phe
1

<210> 35
<211> 4
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic construct

31

<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa is Atc, i.e. 2-aminotetralin-2-carboxylic acid

<400> 35

Tyr Xaa Xaa Phe
1

<210> 36
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<220>
<223> Synthetic construct

<220>
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (4)..(4)

<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<400> 36

Tyr Xaa Phe Phe
1

<210> 37
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<220>
<223> Synthetic construct

<220>
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (4)..(4)
<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<400> 37

Tyr Xaa Trp Phe
1

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<220>
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<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (4)..(4)
<223> AMIDATION

<400> 38

Tyr Xaa Phe Trp
1

<210> 39
<211> 7
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<213> Artificial sequence

<220>
<223> Synthetic construct

<220>
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (7)..(7)
<223> AMIDATION

<400> 39

Tyr Xaa Phe Phe Val Val Gly
1 5

B1

<210> 40
<211> 7
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<220>
<223> Synthetic construct

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (7)..(7)
<223> AMIDATION

<400> 40

Tyr Xaa Phe Phe Tyr Pro Ser
1 5

<210> 41
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<212> PRT
<213> Artificial sequence

<220>

<223> Synthetic construct

<220>
<221> MISC_FEATURE
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<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (7)..(7)
<223> AMIDATION

<400> 41

Tyr Xaa Trp Phe Tyr Pro Ser
1 5

<210> 42
<211> 7
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic construct

81

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (4)..(4)
<223> Phe is Phe(pNO2), i.e. 4-nitrophenylalanine

<220>
<221> MOD_RES
<222> (7)..(7)
<223> AMIDATION

<400> 42

Tyr Xaa Trp Phe Tyr Pro Ser
1 5

<210> 43
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<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic construct

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (6)..(6)
<223> Nle

<220>
<221> MOD_RES
<222> (7)..(7)
<223> AMIDATION

<400> 43

Tyr Xaa Phe Phe Leu Leu Asp
1 5

<210> 44
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<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic construct

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<400> 44

Tyr Xaa Phe
1

<210> 45
<211> 3
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<220>
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<220>
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<222> (2)..(2)
<223> Xaa is Tic, i.e. 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>

<221> MOD_RES
<222> (3)..(3)
<223> AMIDATION

<400> 45

Tyr Xaa Phe
1

<210> 46
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<213> Artificial sequence

<220>
<223> Synthetic construct

<220>
<221> MISC_FEATURE
<222> (2)..(2)
<223> Xaa is Tic-psi-[CH2-], i.e.
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (2)..(3)
<223> nonpeptidyl bond

<400> 46

Tyr Xaa Phe
1

<210> 47
<211> 4
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic construct

<220>
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<222> (2)..(2)
<223> Xaa is Tic-psi-[CH2-], i.e.
3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid

<220>
<221> MOD_RES
<222> (2)..(3)
<223> nonpeptidyl bond

<400> 47

Tyr Xaa Phe Phe
1

<210> 48
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic construct

<400> 48

Tyr Gly Gly Phe Met
1 5

<210> 49
<211> 6
<212> PRT
<213> Artificial sequence

B1

<220>
<223> Synthetic construct

<400> 49

Tyr Gly Gly Phe Met Lys
1 5

<210> 50
<211> 6
<212> PRT
<213> Artificial sequence

<220>
<223> Synthetic construct

<220>
<221> MOD_RES
<222> (1)..(1)
<223> NH2 of Tyr is blocked by butyloxycarbonyl group

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Tyr Gly Gly Phe Leu Lys
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<223> NH2 of Tyr is blocked by butyloxycarbonyl group

<400> 51

Tyr Gly Gly Phe Leu Lys
1 5

<210> 52
<211> 6
<212> PRT
<213> Artificial sequence

<220>
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<220>
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<223> NH2 of Tyr is blocked by butyloxycarbonyl group

<220>
<221> MOD_RES
<222> (6)..(6)
<223> Polymer connected to epsilon-amino group

<400> 52

Tyr Gly Gly Phe Leu Lys
1 5